

Herpes Zoster oticus with multiple cranial nerves involvement: A case series

Ramsay Hunt Syndrome

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Abstract

This case series aims to describe the clinical presentations, management and patient outcomes in four cases of Ramsay Hunt Syndrome (RHS) with multiple cranial nerve involvement. A review of four cases of RHS with a variety of cranial nerve involvement in different age groups (paediatric, adult and elderly) was conducted. The patients were followed up at the otorhinolaryngology outpatient clinic and the response to oral antiviral and steroid therapy was assessed. We observed good responses to combination antiviral-steroid treatment in all 4 cases. There was complete resolution of cranial nerve palsies in 3 out of 4 of the cases within 1-2 weeks. In the remaining 1 case, the symptoms also completely disappeared after 3 months. Relevant clinical and radiological findings were documented. Several theories have been proposed to explain the pathophysiology of other cranial nerve palsies (eg. V, XI, IX, X, XI, and XII) secondary to a Zosterian infection. The described pathways form the basic principles of RHS treatment which involve the usage of oral antivirals and steroid therapies in RHS. There has been some controversy regarding the efficacy of antiviral and steroid therapies in RHS. However, this case series review showed that the combination therapy of antiviral-steroid improved the patients' overall prognosis. Hence, such treatment should be considered in all patients without contraindications.

Keywords

Ramsay hunt; Herpes Zoster; Cranial nerves; Antiviral therapy; Steroid therapy

DOI: 10.4328/ACAM.20369 Received: 2020-10-11 Accepted: 2021-02-18 Published Online: 2021-06-24 Printed: 2021-07-01 Ann Clin Anal Med 2021;12(7):814-818
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Introduction

The Varicella-Zoster virus (VZV) is one of nine herpesviruses known to be capable of infecting human beings. The well-known medical condition it causes is varicella (commonly known as “chickenpox”) as its initial presentation. This infective but self-limiting disease normally presents with a characteristic skin rash consisting of small, itchy, blisters widely distributed over the patient’s back, chest and face. After the primary infection is resolved, the virus resides dormant in the spinal and cranial nerve ganglia lifelong. There is a possibility for the virus to reactivate and replicate subsequently in life, leading to the development of shingles. This occurs as a result of the inflammation caused by the virus as it travels from the affected ganglions through the sensory nerve fibres into the respective dermatomes. This secondary Varicella-zoster viral infection typically presents with the presence of pain and vesicular rash according to its dermatomal distribution. If a patient presents with unilateral otalgia and an eruption of painful, herpetiform skin lesions over the external ear unilaterally, then a clinical diagnosis of herpes zoster oticus (HZO) can be made.

In HZO, the virus arises from the geniculate ganglion of the facial nerve, which consists of sensory, motor and parasympathetic nerve fibres. Following reactivation, neural inflammation, combined with its anatomical location within the petrous temporal bone, may lead to debilitating neurological sequelae, namely, unilateral lower motor neuron facial nerve palsy. [1] This constellation of clinical findings was first described by Ramsay Hunt and since then has been dubbed “Ramsay Hunt Syndrome” (RHS). [2] There have been variations in the way RHS has been defined, however the triad of clinical features include the typical dermatomal distribution of rash (often preceded by pain) and acute peripheral palsy of the 7th cranial nerve on the same side. [1] It is worth noting that the pioneer, Dr. Hunt, himself noticed

the involvement of symptoms such as vertigo and tinnitus, which imply other cranial nerve involvement, namely the 8th cranial nerve. Furthermore, there have been reports of RHS affecting other cranial nerves (albeit less commonly) such as V, VI, IX, X, XI and XII. Sometimes several cranial nerves are simultaneously involved, presenting a clinical picture consistent with that of multicranial neuritis. [1, 3]

The objectives of this manuscript are firstly, to describe the various cranial nerves involvement in RHS and, secondly, to review an adequate treatment protocol for RHS with cranial nerve involvements.

Case Report

Four cases are described in Table 1. Case 1 is a young gentleman with V3, VII and VIII involvement. Case 2 is a paediatric patient with VII and VIII involvement. Case 3 is a middle-aged gentleman with VII, VIII and X involvement. CT reveal fat stranding of the left parapharyngeal space. Case 4 was complicated with facial cellulitis indicating CN V involvement. Informed consent was obtained from all patients for being included in the study.

Discussion

The most commonly affected cranial nerve (CN) involved in RHS is the facial nerve (7th CN). Several theories suggest the pathophysiology of other cranial nerve palsies secondary to a Zosterian infection. Alicandri-Ciuffelli M et al. (2012) [4] hypothesized that the VZV infection spreads between adjacent synapses along the brain stem’s reflex pathways. Anatomically, the nucleus of the facial nerve is in the pons alongside the nuclei of cranial nerves VI and VIII. Also, the proximity of the facial nerve (VII) and vestibulocochlear nerve (VIII) at the level of the cerebellopontine angle (CPA) as they enter the internal auditory canal has been thought to facilitate the virus’ transmission.

Table 1. Summary of patient demographics, cranial nerves involvement, investigations, treatment administered and recovery.

Case	Age (Years)	Presentation	Cranial Nerve Involvement	Investigations	Treatment	Recovery
1	27, gentleman	Vesicular rash over the right cheek for 3 days	Right CN V3 branch Right Lingual nerve CN VIII	Pure Tone Audiometry (PTA): right – moderate sensorineural hearing loss at a mid-high frequency, left – normal hearing. Tympanometry: type A bilaterally.	Oral Acyclovir 800mg 5 times/day for 1 week, IV Dexamethasone 8mg TDS for 3 days, Gabapentin 300mg OD, Lidocaine Lozenges PRN, Difflam Gargle, Paracetamol 1g TDS	1 week after discharge: Vesicular rash resolved. No hearing loss.
2	7, boy	Left otalgia for 1 week with fever and URTI symptoms. A vesicular rash over left ear and left facial asymmetry for 2 days.	Left Facial nerve (HB grade III) CN VIII	PTA: right – normal hearing, left – normal hearing at low frequency, moderate hearing loss at high frequency. Tympanometry: type B bilaterally.	Oral Acyclovir 800mg QID for 1 week, IV Dexamethasone 0.1 mg/kg TDS for 3 days, Syrup Prednisolone 1mg/kg OD for 5 days.	1 week after discharge: vesicular rash resolved. Normal facial nerve function.
3	37, gentleman	Sore throat for 5 days. Left otalgia for 4 days with tinnitus. Left facial asymmetry for 3 days.	Left Facial nerve (HB grade III) CN VIII Left CN X (left vocal cord paresis)	PTA: right – normal hearing, left – mild to moderate sensorineural hearing loss. Tympanometry: right – type A, left – type C. CT head and neck: inflammation of left parapharyngeal space with normal parotid glands.	IV Ceftriaxone 1g BD, Oral Prochlorperazine 5mg TDS, IV Paracetamol 1g TDS, IV Methylprednisolone 500mg STAT then 250mg OD for 2 days, Oral Valacyclovir 1g TDS for 3 days.	Dysphagia resolved at 2 weeks; normal hearing at 2 months. Facial nerve palsy and Vagus nerve palsy resolved completely after 3 months.
4	68, gentleman	Left upper gum swelling for 2 weeks. Left facial swelling, left otalgia and rash over left face for 5 days. No facial asymmetry.	Left facial nerve palsy Left CN V2/V3	PTA: right – mild-moderate sensorineural hearing loss, left – moderate-severe sensorineural hearing loss. Tympanometry: bilateral type B	Oral Acyclovir 800mg 5 times a day for 5 days.	Clinic follow up 1 week after discharge: vesicular rash nearly resolved. Normal facial nerve function.

The specific pathway is believed to be either the vestibulofacial or vestibulocochlear anastomoses. Furthermore, the foramen of Luschka is located inferior-posteriorly to the root entries of CN VII/VIII where the rootlets of origin for CN IX, X, XI lie near to. It is known that anastomoses exist between CN V, VII, IX and X. Inflammation of CN VIII within the internal acoustic meatus may also compress the adjacent CNVIII, resulting in sensorineural hearing loss.

Involvement of the Vagus nerve is rare, but there have been several reports. Postulations include ganglionitis involving adjacent cranial nerves and vascular spread from the infected Carotid sheath/artery. This is in line with the CT findings of the parapharyngeal fat streaking indicating inflammation in case number 3. Another theory is that VZV may cause localized meningitis leading to demyelination in the brainstem [5]. Finally, it is believed that vasculitis-induced infarction of small and large arteries supplying affected cranial nerves may play a role. An example would be a reported case, involving the angiogram findings which revealed occlusion of the ascending pharyngeal artery, which supplies CN IX-XII. The described pathophysiological pathways of RHS form the basic principles of treatment for this condition, which involves the usage of oral antivirals and steroid medications.

Antiviral agents such as Acyclovir, Famiciclovir, Penciclovir, and Valacyclovir belong to a group of medications called “nucleoside analogues” and work by inhibiting the viral replication process directly thereby reducing the severity and subsequent complications of the VZV infection. In fact, post-herpetic neuralgia (PHN) is one of the most common sequelae, and it can be prevented if antiviral therapy is initiated promptly. Furthermore, antiviral therapy may decrease the duration of new vesicle formation and the time for vesicles to become crusted. However, it is worth noting that treatment is most effective if started within the first 72 hours of the onset of rash. According to the European Consensus-based (S2k) Guideline on the Management of Herpes Zoster (2016) [6], there have been a limited number of studies conducted to evaluate the efficacy of treatment 72 hours after onset of rash. However, the panel of experts still suggests to initiate antiviral medications (even after 72 hours of onset of symptoms) in the following cases: the appearance of new vesicles, patients with complications or at risk of developing complications, signs of cutaneous, visceral or neurological dissemination, cases of Herpes Zoster oticus/ ophthalmicus and in all immunocompromised patients [6]. In this consensus, the duration of antivirals suggested is as long as no new vesicular skin lesions appear.



Figure 1. Case 1: Vesicular rash along right cranial nerve V3 distribution.

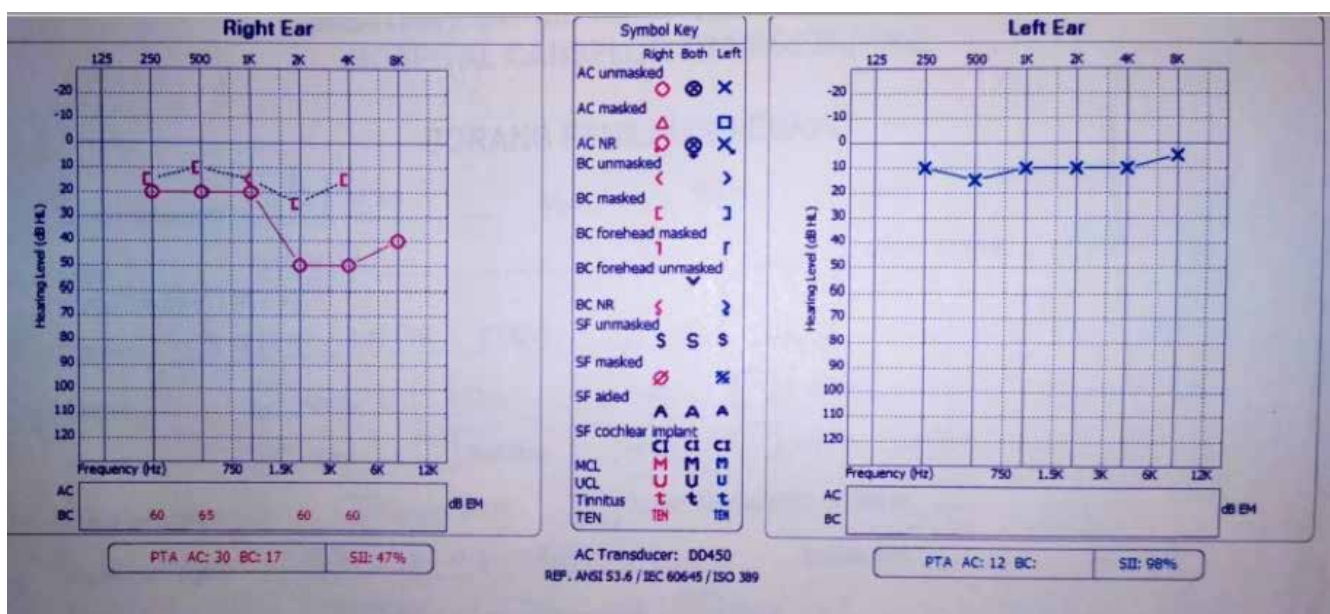


Figure 1a. Case 1: Patient’s pure tone audiogram. Right: moderate SNHL at mid-to-high frequency. Left: normal hearing.



Figure 2. Case 2: At clinic follow-up, 1 week after discharge, showing resolved left facial nerve palsy.



Figure 3. Case 4: Vesicular rash along left cranial nerve V2/3 distribution. Anterior view (left pic) and left lateral view (right pic).

The use of corticosteroids in VZV infections is controversial, for there have been studies to suggest that short-term regimens may have benefits such as reducing the incidence of PHN. On the other hand, there are some studies which show steroids have no advantage. Corticosteroids such as Prednisolone and Methylprednisolone have an anti-inflammatory effect, which has been suggested to aid in restoration of facial nerve function. The European Consensus quoted earlier, recommends combined therapy of intravenous Aciclovir and systemic corticosteroids in Herpes Zoster Oticus with facial nerve involvement or with severe pain and other cranial nerve palsies. Steroids play an important role in reducing the viral-induced inflammation of the facial nerve [7].

Combination therapy is more effective in the recovery of facial nerve function and gives a better prognosis. One systematic review revealed that the combination of steroids and Acyclovir reached better recovery rates when compared to monotherapy with steroids only, with a better prognosis of facial nerve palsy on earlier commencement. Various steroid regimens have been proposed, however, the clinician may consider giving an initial loading dose (to gain control of skin condition) eg. 40-60mg daily (0.5-1.0 mg/kg) for 7-10 days with the dose gradually tapered down [8].

Conclusion

Herpes Zoster Oticus most commonly involves cranial nerves VII and VIII, although it may also involve various other cranial nerves simultaneously in complicated cases. We recommend that all patients with Ramsay-Hunt Syndrome should be considered for combination therapy of antiviral-steroid in order to improve the patient's overall prognosis. As usual, any contraindications must first be excluded to determine patient's suitability.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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How to cite this article:

Oui Ting Jie, Mawaddah Azman, Balwant Singh Gendeh, Hardip Singh Gendeh. Herpes Zoster oticus with multiple cranial nerves involvement: A case series. *Ann Clin Anal Med* 2021;12(7):814-818